Modern Biology: A Terrifying Power

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In the past twenty years, one has heard much talk of a biological revolution and of its consequences for mankind—not only in medical and economic achievement but in the nature of man itself. Man may soon be able to influence his own heredity directly, rather than only by the indirect process of eugenics. Scientists and science writers discuss such prospects with an uneasy mixture of optimistic predictions of benefits to come and dire warnings of possible catastrophes—as in Desmond Taylor's *The Biological Time Bomb.* Here I shall attempt to examine briefly the scientific basis of the expected developments, their probable nature, and the responsibility they present to both scientists and the public.

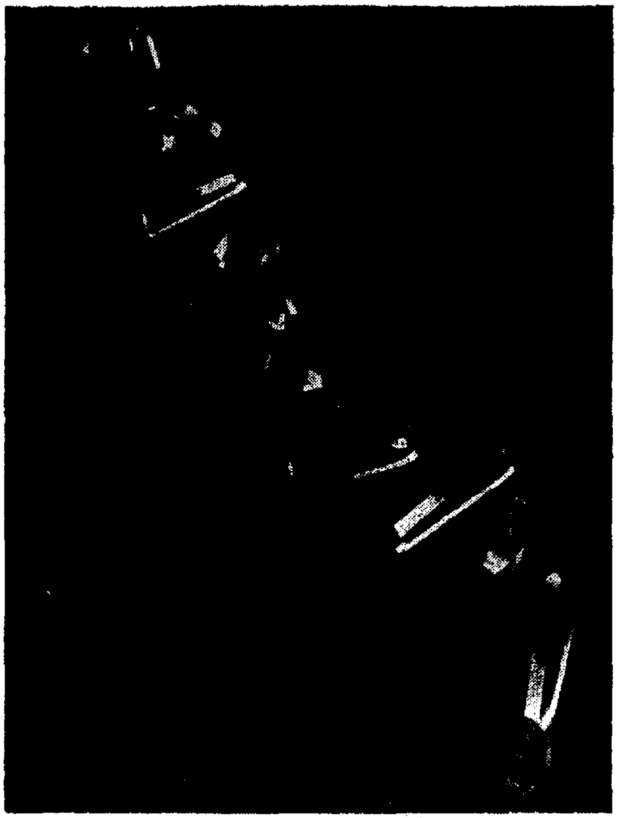
What has happened in biology in the last two decades is not a revolution but a scientific fulfillment. Modern biology started about 100 years ago with the foundation of Darwin's theory of evolution, which ties together all living organisms, past, present and future, into a single historical process of parenthood. The achievement of the last decades is the understanding of the nature, function and changes of the organic substrate of evolution, *the genetic material*, which is the stuff that carries from one generation to the next the set of instructions that dictate what an organism is, how it responds, and what kind of descendants it will in turn produce.

By 1952 the material of the genes was identified chemically as consisting of nucleic acid—generally (except in some viruses) desoxyribonucleic acid or DNA. In 1953 Watson and Crick proposed for the structure of DNA a model—the famous double helix—which not only proved to be correct but opened up entire new approaches to the study of the chemistry of heredity. Within the last sixteen years biologists have come up with the following satisfactory picture of what genes are and how they function.

A gene is a certain stretch in a long DNA fiber contained in the chromosomes of the cell nucleus. It carries in chemical imprint the detailed instructions for making both new copies of itself at each cell division and disposable "subcopies" or messages, which are used as instructions for synthesizing all the machinery of the cell. The messages are molecules of another kind of nucleic acid called RNA.

Gene structure and gene function are not immutable—if they were, evolution and development could not take place. On the one hand, the structure of genes can change by mutation, a relatively rare accidental change in chemical composition. Natural selection then brings about evolution by selecting for reproductive success those individuals endowed with particular genetic constitutions. On the other hand, the function of the genes in a cell is regulated by the environment, including the action of other genes in the same cell, the chemical messages from other cells, and also the external environment such as food and temperature. Thus while all cells of a complex organism have identical sets of genes (barring rare mutations), they function differently because some of their genes (which may number from a few thousand to several million, depending on the organism) receive different environmental signals.

The relevant point for this article is that all the essential features of the genetic process, insofar as they have been clarified, have turned out to be interpretable in strictly biochemical terms. No new principle or phenomenon has emerged to justify the assumption that some unique "vitalist" principle is at work in biological processes. This point is essential to a grasp of the present status and future course of biological technology. What molecular biologists have done is to make the genetic mechanism directly available to chemical experimentation. Arthur Kornberg and other biochemists have purified DNA from bacteria, viruses and from animal cells, including human cells. They have then caused it to produce more copies of itself in the test tube, under the influence of enzymes extracted either from the same organism or



Detail of DNA Molecule

from other organisms. At the time of this writing, Ghobind Khorana is perfecting the chemical synthesis of a gene in the test tube. The chemical mechanisms of gene mutation have been clarified. The process of making gene messages, and the use of these messages to produce the individual pieces of cell machinery, have been duplicated and analyzed in the test tube. The nature of the chemical signals—the regulatory substances that turn on and off specific genes—is now known, at least in bacteria. Biochemists have purified some of these regulatory substances and demonstrated their actual attachment to the specific genes that they block or unblock.

Obviously such knowledge, which reaches to the most intimate level of the hereditary mechanism, can generate a new and powerful genetic technology. The traditional technology was applied in agriculture and husbandry to breeding desirable varieties of crops and animals, and in medicine to understanding, diagnosing and treating such genetic disorders as hemophilia, diabetes and phenylketonuria. Social application of classical genetics in the form of human eugenics has been advocated but seldom carried out. The selective elimination of genetic defects by restraining procreation on a voluntary basis has never found much favor. Positive "germinal selection"—that is, the spreading of exceptionally desirable sets of genes through sperm banks and artificial insemination—was advocated forcefully by the great geneticist, H. J. Muller, but has encountered many objections, including the ethical problems of who is to decide what is desirable in human heredity. In any case, germinal selection gives at best improved odds for superior progeny: the lottery of genetics—the random distribution of chromosomes and genes of each parent into different sperm cells or eggs—makes this process slow and inefficient.

In *Brave New World*, his nightmarish utopia of a conditioned humanity published in 1932, Aldous Huxley foresaw for the year 600 "After Ford" a type of eugenics based on artificial fertilization, twinning induced in the test tube, chemical conditioning of the growing embryos, and psychological conditioning of the growing children. Some of the embryological techniques imagined by Huxley, and others even more powerful, are rapidly approaching reality. For example, artificial fertilization of human eggs has been recently achieved in the test tube by Edwards and his co-workers in England. The separation and reshuffling of the cells of fertilized mouse eggs in course of division, followed by reimplantation and normal birth, has been accomplished by Beatrice Mintz. And more than twenty years ago, the nucleus of an unfertilized frog egg was replaced with the nucleus of an adult cell—a process that could produce at will large numbers of truly identical twins. It may soon become routinely feasible with mammals, including man. Thus, at least in principle, Huxley's made-to-order human being has become feasible much sooner than he anticipated.

But these embryological methods represent only a relatively clumsy, unrefined technology when compared to the one promised (or threatened) by true genetic surgery—the artificial correction, replacement, removal or addition of genes, based on the discoveries of molecular biology. A coupling of genetic intervention with embryological surgery would open the way to truly awesome possibilities. The actual applications are admittedly still very distant; but I believe it is not too soon to become aware of the prospects.

Here are some of the relevant facts. In bacteria, which are used most frequently for this kind of research, it is already possible to introduce genes or groups of genes as purified pieces of DNA molecules. Under appropriate conditions, these genes enter the cells with a high chance of replacing the corresponding resident genes. Thus a bacterium that is sensitive to streptomycin, for example, can be "transformed" to being resistant to streptomycin by replacement of the appropriate gene. The descendants of such a transformed bacterium are all resistant. When this process of gene replacement is carried out with unsorted DNA fragments it is very inefficient; but there are methods, still being perfected, for sorting out DNA fragments to correspond with individual genes or groups of genes. I mentioned before that the chemical synthesis and copying of genes in the test tube is also becoming possible. It is clear, therefore, that the ability to manufacture large amounts of any specific gene may soon, like all purely technical achievements, become only a matter of investing sufficient money and personnel.

The introduction of specific genes into human cells, especially in the cells of the germ line that give rise to sperm and egg, is still far from actuality. But developments that may lead in that direction are already at hand. Thus, at least in bacteria, some mild viruses can pick up one or more genes from the cells in which they have grown and transfer them to other cells. Then these genes may either replace the resident ones or become added, more or less permanently, to the gene set. In some cases the added genes upset the regulation of their new host, for example, by inhibiting the function of certain other genes.

Besides viruses, there are other, even less destructive, agents called episomes or plasmids, which in bacteria can transfer and add genes from one cell to another. It would not be surprising if similar phenomena were soon to be discovered in the cells of animals and of man, where they would provide a way to add or replace genes. In fact, some viruses that produce tumors in animals (and possibly also in man) have certain properties of the gene-transferring viruses. A major barrier to genetic intervention will be, of course, the difficulty of manipulating the germ cells It is conceivable, however, that gene-carrying viruses could be made specific for the germ cells. Even the injection of DNA molecules into eggs in the course of artificial fertilization may become possible.

What kind of applications can we foresee for the discoveries that I have just outlined? By and large, they fall into four groups: medical, bio-industrial, social and military.

In medicine, we may envisage replacing the present treatments of genetic defects—for example, insufficient production of a hormone such as insulin—by supplying the proper gene to certain cells from the outside, or by implanting functional cells, or by causing the corresponding gene to become activated in other cells of the body which normally do not produce the hormone because of regulatory repression. Manipulations of this kind could also, for example, alter the immunological reactions that cause the body to reject foreign tissue, an achievement that would make organ transplants much more successful.

In the bio-industrial field, it might be possible to use direct genetic manipulation instead of selective breeding to manufacture more desirable or healthier strains of a variety of organisms, from yeasts to cereals to cattle, by implanting or removing specific genes or chromosomes.

With social applications, we enter the truly controversial field. If it becomes possible to manipulate the genes of the human germ line or to achieve artificial fertilization and nuclear transplantation with human eggs. we would be faced with the terrifying responsibility of deciding what we—the human race—intend to become. At the start, we may simply remove defective genes or replace them with their normal counterparts. Then we may start to fool around by introducing supposedly "desirable" genes. We may even be tempted to manufacture many identical copies of a supposedly "superior" individual; for example, by introducing identical nuclei from its cells into series of enucleated eggs, which may then be implanted in the wombs of foster mothers.

At this point, ethical and legal problems of a completely new nature and magnitude arise Who is to decide what is desirable or undesirable, superior or inferior, in a man? The doctor? The state? And beyond that, what ethical and legal criteria would apply to human beings who are not born by a natural process but are the product of deliberate genetic manipulation? When does a "repaired" or "manufactured" man stop being a man (whatever that means) and become a robot, an object, an industrial product?

I shall refrain here from speculating on possible genetic weapons. Whereas the obstacles in the way of supposedly constructive genetic surgery are very great (but *not* insurmountable), the obstacles to destructive uses may be smaller, if only because any one of many possible noxious results may be "desirable" in the military sense. Thus, for example, we may witness efforts to invent viruses that can spread in an enemy population genes that produce sensitivity to poisons, or susceptibility to tumors, or even transmissible genetic defects—in other words, genetic genocide. The development of pathogenic germs resistant to certain antibiotics has been going on for years in the biological arsenals of "civilized" countries.

Finally, we should not ignore the possibility that genetic means of controlling human heredity will be put to massive uses of human degradation even outside the military context. Huxley's nightmarish society might be achieved by genetic surgery rather than by conditioning, and in an even more terrifying way since the process would be hereditary and irreversible.

The situation that I have tried to project, based on biological developments which are either current or reasonably predictable, is not unique to biology. Whenever a science develops to the point of generating new technology, it presents society with a mixed bag of opportunities and risks. The question that faces society is not that of feasibility. Once the scientific principles are established, technological application is almost certain to come. Thus, faced with the prospect of a new genetic technology, we must ask ourselves as soon as possible whether and how it will be used and what can we do about it. Optimists and pessimists differ. Robert Sinsheimer, of the California Institute of Technology, stresses "the chance to ease the internal strains and heal the internal flaws directly." Rollin Hotchkiss, of Rockefeller University, warns that in putting the new genetic technologies to supposedly constructive uses, "the pathway will, like that leading to all of men's enterprise and mischief, be built from a combination of altruism, private profit, and ignorance." But they both stress the need "to prepare now for the new reality" and "to caution an impatient altruism, curb an overenthusiastic self-interest, or offset an uninformed interventionism." These concerns have to do, of course, with the constructive possibilities. The destructive ones, military or otherwise, would be welcomed only by the most narrow-minded, Neanderthal type of rabid nationalist or totalitarian.

What can we do about it? The least rational and least effective approach would be to advocate a moratorium on science in order to prevent the rise of potentially misapplicable technologies. The human cultural enterprise depends on freedom of inquiry. Science, like the arts, has become an inseparable part of the intellectual adventure of man. What is needed, rather, is a rational machinery, both national and international, to determine sensible policies and priorities in the application of scientific knowledge. The present absence of such machinery is sadly reflected in the way decisions are made on major programs such as the man-on-the-moon venture. Even more relevant and more frightening is the apparent inability of organized society to cope with the menace of overpopulation, a threat greater than that of nuclear self-destruction.

Whether or not a rational decision-making machinery can be achieved within society as it is now structured, either in the United States or in any other country, remains to be seen. A recently published report of a Panel on Technology of the National Academy of Sciences deals with some of the issues in a constructive way Its limited range of recommendations, however, provides little comfort to those who feel that the problems of technology and human life require radical action by informed and responsible governmental bodies.

Basically, we need to create a society in which technology is purposefully directed toward socially chosen goals. This is a political rather than a scientific task, and scientists can hardly be expected to provide the solution. What they can and must do, however, is face the problems within their own sphere of activity.

On the negative side, scientists can make a conscious effort not to promote or encourage technological development without having first faced and resolved in their own minds the social implications. On the positive side, scientists must assume the responsibility to tell society, in a forceful and persistent manner, what science is discovering and what the technological consequences are likely to be. We ought not to be deterred by the widespread and increasing ignorance of the public, including governments, in scientific matters, but rather should strive to break through that barrier Long-term educational programs may be inadequate because time is short. Faster ways must be found to convey the practical implications of the modern world of science to the scientifically uncivilized public consciousness.

If these responsibilities, however limited, are to be met, most scientists must undergo a major change of attitude. I believe that such change can be brought about because the present and forthcoming realities—whether those of an overpopulated world or of a humanity that can remake itself in whatever image it chooses—are stirring and disturbing the imagination of more and more scientists. Still, active leadership will be needed to develop and crystallize within the scientific milieu an enhanced concern for the social consequences of science and for the responsibilities of its practitioners. Even more important, this leadership must find the way to awaken the public and their elected representatives from the complacency that lies behind the distorted priorities of present-day society.